REMARKS

Applicants request entry of this Amendment and reconsideration of the rejection of the claims.

Claims 2-4, 8-11, 15, 16, 18-21, and 96-106 are currently pending. Claims 9, 96, 99, 102 and 103 are amended. Applicants submit the amendments are supported throughout the specification, including at page 133, line 16 to line 29; page 152, line 25 to page 153, line 1; Figure 5, page 8, line 27 to page 9, line 5; page 12, line 15 to page 13, line 15; and page 10, line 18 to line 25.

Priority

Applicants claim domestic priority under 35 U.S.C. § 119(e) to U.S. Serial No. 60/228,914, filed August 29, 2000, U.S. Serial No. 60/197,089, filed April 14, 2000, and U.S. Serial No. 60/175,849, filed January 13, 2000. Applicants contend these provisional applications provide adequate support under 35 U.S.C. § 112 for the SEQ ID NOs of the instant invention. For example, Applicants teach SEQ ID NO:1 and SEQ ID NO:2 at, *inter alia*, page 5, lines 10-12 and 16-18, page 6, lines 3-5 and 8-9; page 7, line 31 to page 8, line 2; page 8, lines 7-10 and 17-19; page 20, lines 13-20; Figures 1 and 2 of U.S. Serial No. 60/228,914. More particularly, Applicants teach the specific nucleotide of SEQ ID NO:1 and amino acid sequence of SEQ ID NO:2 in Figures 1 and 2, respectively, of U.S. Serial No. 60/228,914. Applicants teach the specific nucleotide of SEQ ID NO:1 and amino acid sequence of SEQ ID NO:2 at, *inter alia*, page 20, lines 13-20; Figures 1 and 2, respectively, of U.S. Serial No. 60/197,089. Applicants teach the specific nucleotide of SEQ ID NO:1 and amino acid sequence of SEQ ID NO:2 at, *inter alia*, page 14, lines 17-24; Figures 1 and 2, respectively, of U.S. Serial No. 60/175,849.

Based on the foregoing support, Applicants respectfully request acknowledgement of Applicants' claim for domestic priority under 35 U.S.C. § 119(e) to U.S. Serial No. 60/228,914, filed August 29, 2000, U.S. Serial No. 60/197,089, filed April 14, 2000, and U.S. Serial No. 60/175,849 filed, January 13, 2000.

IDS Submissions

Applicants have submitted Supplemental IDS statements on Sept. 13, 2001 and October 20, 2004. Applicants provide a courtesy copy of the IDS submitted on September 12, 2001. Applicants also submit herewith a Supplemental IDS. Applicants request consideration of all of the references and return of the initialed 1449 forms.

Rejection Under 35 U.S.C. § 112, Second Paragraph, Indefiniteness

Claims 96 and 99 have been rejected under 35 U.S.C. § 112, first paragraph, for alleged indefiniteness. The Examiner contends that the figures and specification do not clearly identify the sequence of the transmembrane domains. Applicants respectfully traverse.

Applicants submit that one of skill in the art reading the specification would understand that the polypeptide encoded by the claimed nucleic acid sequence has 9 transmembrane domains. These domains are identified in Figure 2 and also shown in Figure 9. Applicants have also provided the amino acid sequence of SEQ ID NO:2 and identified the boundaries of the transmembrane domains at page 10, lines 18-25. Thus, Applicants submit that one of skill in the art would clearly understand the amino acid sequence of the transmembrane domains.

Thus, Applicants respectfully request withdrawal of the rejection on this basis.

Rejection Under 35 U.S.C. § 112, First Paragraph, New Matter

Claims 9-11 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. According to the Office Action, claim 9 introduces new matter by reciting that isolated nucleic acids encoding a PRO10282 peptide are at least 100 amino acids in length. Applicants respectfully traverse the rejection.

While not acquiescing in the rejection and solely to expedite prosecution, Applicants have amended claim 9 to indicate that the isolated nucleic acid comprises at least 900 nucleotides. Applicants submit that this amendment does not raise any issues of new matter as the specification clearly contemplates and describes nucleic acid molecules of different lengths that can hybridize to a complement of the nucleic acid sequence that

encodes amino acids 1 to 667 of Figure 2. (See specification at page 12, line 15 to page 13, line 14.)

Thus, Applicants submit the specification provides sufficient written description to show possession of the claimed invention, and respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph, rejection.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 96, 99, and 100-106 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Office Action alleges that there is no description of the genus of PRO10282 polypeptides having the nine potential transmembrane domains identified in Fig. 9. The Office Action also alleges there is no description of the genus of PRO10282 polypeptides that would bind an antibody raised against SEQ ID NO:2. According to the Office Action, there is no description of epitopes of SEQ ID NO:2 recognizable by an antibody against protein SEQ ID NO:2; thus there is no description of the genus of PRO10282 polypeptides that would bind an antibody raised against SEQ ID NO:2. Applicants respectfully disagree.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. *Vas-Cath Inc. v. Mahurkar,* 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter ***sufficient to distinguish it from other materials***. *Univ. of California v. Eli Lilly and Co.,* 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can ***identify many of the species*** that the claims encompass, such a formula is normally an adequate description of the claimed invention. *Id.* at 1406 (emphasis added). Applicants can also satisfy the written description by providing partial structure, physical and chemical properties, functional characteristics, known or disclosed correlation between structure and function, methods of making and combinations thereof. (See the Guidelines for Written Description at page 8.)

Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) *Fed Reg.* 1099, 1105 (2001); *see also, In re Wertheim,* 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a ***preponderance of evidence*** why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) *Fed. Reg.* at 1107; 191 USPQ at 97, (emphasis added).

As discussed previously, Applicants submit the specification does describe the transmembrane domains of the human Stra6 polypeptides. Applicants have shown the locations of the transmembrane domains of each of the human polypeptides in Figures 2 and 7. The specification further shows a hydrophobicity plot in Figure 9. The specification describes the amino acid sequences corresponding to these domains at page 10 in the specification. The specification also indicates that these transmembrane domains are conserved in the mouse Stra6 amino acid sequence. Applicants submit that one of skill in the art reading the specification would understand that Applicants have adequately described and were in possession of the claimed nucleic acids.

Claim 102 relates to an isolated nucleic acid molecule which comprises DNA having at least 99% sequence identity to (a) a DNA molecule encoding a PRO10282 polypeptide comprising the sequence of amino acid residues 1 to 667 of SEQ ID NO:2, wherein the isolated nucleic acid molecule encodes a polypeptide which binds an antibody raised against PRO10282 polypeptide comprising the sequence of amino acid residues 532 to 667 of SEQ ID NO:2 and which is expressed on the cell surface. In a parallel manner, claim 103 relates to a an isolated nucleic acid molecule which comprises DNA having at least 99% sequence identity to (a) the full length polypeptide coding sequence of ATCC deposit no. PTA-1181, wherein the isolated nucleic acid molecule encodes a polypeptide which binds an antibody raised against PRO10282 polypeptide comprising the sequence of amino acid residues 532 to 667 of SEQ ID NO:2 and is expressed on the cell surface.

Applicants teach methods for preparation of antibodies that bind PRO10282 and methods for purification of PRO10282 polypeptides using specific antibodies (*see*, Examples 7 and 8, pages 132-135 of the specification). Applicants contend one skilled in the art would immediately recognize the PRO10282 polypeptides that bind an antibody against protein SEQ ID NO:2 based on Applicants' teachings. For example, one skilled in the art could obtain such PRO10282 polypeptides by purification of cell lysate over an anti-SEQ ID NO:2 immunoaffinity column as described in Example 8. One skilled in the art could easily prepare antibodies that bind SEQ ID NO:2 (anti-SEQ ID NO:2 antibodies) for such an immunoaffinity column using the methods set forth by Applicant in Example 7, or by antibody production methods that are well-known in the art. Based on the examples and methods provided, Applicants contend the specification contains sufficient description of PRO10282 polypeptides that would bind an antibody raised against SEQ ID NO:2.

Moreover, Applicants have described production of monoclonal antibodies to a polypeptide comprising the amino acid sequence of 532 to 667 of human Stra6. (See the specification at page 133, line 16 to page 134, line 2.) Applicants have also shown that antibodies to human Stra6 can detect cell surface protein on colorectal cancer cells and that the staining intensity with the monoclonal antibodies was increased after the treatment of the cells with retinoic acid. (See the specification at page 152, line 25 to page 153, line 1.)

Thus, Applicants submit the specification provides sufficient written description to show possession of the claimed invention, and respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph, rejection.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 9 and 10 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. According to the Office Action, the specification, while being enabling for the nucleotide sequence of SEQ ID NO:1, does not reasonably provide enablement for polynucleotides having a certain degree of hybridization to the

polynucleotide SEQ ID NO:1 because there is not sufficient guidance as to how to use the polynucleotides. Applicants respectfully traverse the rejection.

The legal standard for enablement under 35 U.S.C. § 112 requires that "[...] a patent specification must disclose sufficient information to enable ***those skilled in the art*** to make the claimed invention." *Hormone Research Foundation, Inc. v. Genentech*, 15 USPQ2d 1039, 1047 (Fed. Cir. 1990). It is a well accepted premise that §112, ¶1 requires only that a patent specification describe to one of ordinary skill in the art how to make and use the claimed invention without ***undue*** experimentation.

The Examiner acknowledges that the specification is enabling for the nucleotide sequence of SEQ ID NO:1 (which encodes protein SEQ ID NO:2) (*see*, page 7 of the Office Action). In addition to the nucleotide sequence of SEQ ID NO:1, claims 9 and 10 also encompass polynucleotides encoding a PRO 10282 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence that encodes amino acids 1 to 667 of SEQ ID NO:2. The Office Action's contention that lack of expression information for polynucleotides other than SEQ ID NO:1 encompassed by the claims invention does not support an enablement rejection.

Applicants agree with the Examiner that the specification teaches that the polynucleotide of SEQ ID NO:1 is over-expressed in cancer tissues and thus can be used in cancer diagnostics. However, Applicants disagree with the Office Action basing the rejection at least in part on the alleged lack of information about over expression of other polynucleotides. Under the law of enablement, a specification that teaches how to make and use the invention in terms, which correspond, in scope to the claims must be taken as satisfying the enablement requirement unless there is reason to doubt the objective truth of the specification. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). It is incumbent upon the Examiner to explain why one skilled in the art would doubt the truth of statements made in the specification, and provide back up assertions with acceptable evidence or reasoning which is inconsistent with the teachings of the specification. *Id.* at 370. Absent evidence to the contrary, the specification must be assumed to be enabling.

Claims 9 and 10 are further supported by a naturally occurring variant, PRO19578 shown in Figures 6 and 7 (SEQ ID NO:4) that has less than 100% nucleotide

sequence identity to SEQ ID NO:1. The alignment between amino acid sequence (SEQ ID NO:2), the variant (SEQ ID NO:4), and the murine stra6 sequence identifies regions of high identity of the molecule. One of skill in the art would immediately recognize that SEQ ID NO:4 would hybridize to the complement of the polynucleotide of SEQ ID NO:1 based on the nucleotide sequence identity. The use of the variant sequence is also supported in the specification to allow one of skill in the art to make and use it. For example, Example 2 at page 121 provides a method of using PRO19578 as a hybridization probe. For the description of the variant sequence, one of skill in the art can make use of this and other variants in the same manner as SEQ ID NO:1. It is routine for one skilled in the art to identify nucleic acid molecules capable of use for detecting a target polynucleotide.

Thus, Applicants submit that they have provided sufficient description to allow one of skill in the art to make and use the claimed nucleic acids, and respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph, rejection.

Rejection Under 35 U.S.C. § 102

Claims 9-11 have been rejected 35 U.S.C. § 102(a) as allegedly anticipated by the sequence of Database GenEmbl, Accession No. AAV84436. The Office Action alleges that the alignment covers nucleotides 1768-2663, not 1768-2049 as indicated by Applicants. Applicants respectfully traverse the rejection.

Applicants' claim 9 recites an isolated nucleic acid that comprises at least 900 nucleotides and that encodes a PRO10282 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence that encodes amino acids 1 to 667 of Figure 2 (SEQ ID NO:2).

For the reasons discussed previously, Applicants do not agree with the Examiner's position regarding claim 9. While not acquiescing in the rejection and in order to expedite prosecution, Applicants have amended the claim to indicate the isolated nucleic acid comprises at least 900 nucleotides. The nucleic acid of AAV84436 has less than 900 nucleotides. For at least this reason, Applicants submit that AAV84436 does not anticipate the claimed invention.

Based on the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(a) rejection.

Double Patenting

Applicant defers commenting on any double patenting rejections until an actual rejection is presented.

Request for an Interview

Applicants request an interview with the Examiner and his supervisor.

CONCLUSION

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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